

WHAT IS CLAIMED IS:

1. A method for close-range lesion detection, during an operative, intravascular, laparoscopic, or endoscopic procedure, wherein the method comprises:

(a) injecting a patient subject to such a procedure parenterally with an effective amount of a labeled divalent single chain antibody fragment or subfragment with a molecular weight of 85,000 daltons or less, which specifically binds an antigen produced by or associated with a lesion;

(b) conducting the procedure within 48 hours of the injection;

(c) scanning the accessed interior of the patient at close range with a detection means for detecting the presence of the labeled antibody fragment or subfragment; and

(d) locating the sites of accretion of the labeled antibody fragment or subfragment by detecting elevated levels of the labeled antibody fragment or subfragment at such sites with the detection means.

2. The method of claim 1, wherein said the procedure is conducted within 24 hours of the injection.

3. The method of claim 1, wherein the procedure is conducted within 12 hours of the injection.

4. The method of claim 1, wherein the procedure is conducted within 6 hours of the injection.

5. The method of claim 1, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation, a clot, hyperplasia and atherosclerotic plaque.

6. The method of claim 1, wherein the fragment or subfragment is monospecific.

7. The method of claim 1, wherein the fragment or subfragment is bispecific.

8. The method of claim 1, wherein the fragment or subfragment has a molecular weight of 65,000 daltons or less.

9. The method of claim 1, wherein the fragment or subfragment has a molecular weight of 55,000 daltons or less.

10. The method of claim 1, wherein the fragment or subfragment has a molecular weight of 50,000 daltons or less.

11. The method of claim 1, wherein the label for the fragment or subfragment is a radioisotope that emits at an energy of 20-1,000 kev.

12. The method of claim 11, wherein the radioisotope is selected from the group consisting of technetium-99m, iodine-125, iodine-131, iodine-123, indium-111, and gallium-67.

13. The method of claim 1, wherein the label of said labeled antibody fragment or subfragment is a non-isotopic agent.

14. The method of claim 13, wherein the non-isotopic agent is a photoactive agent.

15. The method of claim 14, wherein the photoactive agent is a fluorescent agent.

16. The method of claim 1, wherein the method further comprises treating detected sites during the procedure.

17. The method of claim 1, wherein the procedure is an operative procedure.

18. The method of claim 1, wherein the procedure is an intravascular procedure.

19. The method of claim 1, wherein the procedure is an endoscopic procedure.

20. The method of claim 1, wherein said procedure is a laparoscopic procedure.

21. The method of claim 1, wherein said procedure is a biopsy, and the biopsy implement is guided to lesions at sites of elevated label accretion.

22. The method of claim 1, further comprising treating the lesion during the procedure by brachytherapy, external beam radiation, laser therapy or surgical removal.

23. The method of claim 1, wherein the location of sites of accretion is performed without the use of a clearing agent, contrast agent or subtraction agent.

24. A method of detection of lesions during an endoscopic, laparoscopic, intravascular catheter, or surgical procedure, wherein the method comprises:

injecting a patient to undergo such a procedure with a divalent single chain antibody fragment or subfragment with a molecular weight of 85,000 Daltons or less, labeled with a fluorescent agent or dye, wherein the labeled antibody fragment or subfragment accretes at the lesion;

permitting the labeled antibody fragment or subfragment to accrete;

conducting the procedure within 48 hours of the injection; and

detecting the label with a light source supplied via an endoscope, laparoscope, or intravascular catheter or during the surgical procedure.

25. The method of claim 24, further comprising the step of removing lesions at sites of elevated label accretion with a laser or surgically.

26. The method of claim 25, further comprising the step of treating lesions at sites of elevated label accretion with ionizing radiation.

27. The method of claim 26, wherein the procedure is selected from the group consisting of an endoscope, laparoscope, and intravascular catheter procedures, further comprising the step of administering brachytherapy via the endoscope or catheter to lesions at sites of elevated label accretion.

28. The method of claim 24, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation lesion, a clot, hyperplasia and atherosclerotic plaque.

29. The method of claim 24, wherein the fragment or subfragment is monospecific.

30. The method of claim 24, wherein the fragment or subfragment is bispecific.

31. The method of claim 24, wherein the fragment or subfragment has a molecular weight of 65,000 daltons or less.

32. The method of claim 24, wherein the fragment or subfragment has a molecular weight of 55,000 daltons or less.

33. The method of claim 24, wherein the fragment or subfragment has a molecular weight of 50,000 daltons or less.

34. The method of claim 24, wherein said procedure is conducted within 24 hours of the injection of said labeled antibody fragment or subfragment.

35. The method of claim 24, wherein said procedure is a laparoscopic procedure.

36. The method of claim 24, wherein the label is detected without the use of a clearing agent, contrast agent or subtraction agent.

37. A method of detection and treatment of lesions during an endoscopic, laparoscopic, or intravascular catheter procedure, wherein the method comprises:

(a) injecting a patient to undergo such a procedure with a divalent single chain antibody fragment or subfragment with a molecular weight of 85,000 Daltons or less, labeled with an agent capable of detection, which labeled antibody fragment or subfragment preferentially accretes at the lesion;

(b) permitting the labeled antibody fragment or subfragment to accrete at the lesion;

(c) conducting the procedure within 48 hours of the injection;

(d) detecting the agent with a detection means supplied via the endoscope, laparoscope, or intravascular catheter; and

(e) treating the lesion by brachytherapy administered through the endoscope or intravascular catheter.

38. The method of claim 37, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation lesion, a clot, hyperplasia and atherosclerotic plaque.

39. The method of claim 37, wherein the fragment or subfragment is monospecific.

40. The method of claim 37, wherein the fragment or subfragment is bispecific.

41. The method of claim 37, wherein the fragment or subfragment has a molecular weight of 65,000 daltons or less.

42. The method of claim 37, wherein the fragment or subfragment has a molecular weight of 55,000 daltons or less.

43. The method of claim 37, wherein the fragment or subfragment has a molecular weight of 50,000 daltons or less.

44. The method of claim 37, wherein said procedure is conducted within 24 hours of the injection of said labeled antibody fragment or subfragment.

45. The method of claim 37, wherein said procedure is a laparoscopic procedure.

46. The method of claim 37, wherein the label is detected without the use of a clearing agent, contrast agent or subtraction agent.

47. A method of treatment of lesions during a laparoscopic or intravascular catheter procedure, wherein the method comprises:

injecting a patient to undergo such a procedure with a divalent single chain antibody fragment or subfragment with a molecular weight of 85,000 Daltons or less, labeled with a photoactive agent, wherein the antibody fragment or subfragment preferentially accretes at targeted lesions;

permitting the labeled antibody fragment or subfragment to accrete;  
conducting the procedure within 48 hours of the injection; and  
activating the photoactive agent with a light source supplied via the laparoscope or intravascular catheter, thereby treating said lesions.

48. The method of claim 47, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation lesion, a clot, hyperplasia and atherosclerotic plaque.

49. The method of claim 47, wherein the fragment or subfragment is monospecific.

50. The method of claim 47, wherein the fragment or subfragment is bispecific.

51. The method of claim 47, wherein the fragment or subfragment has a molecular weight of 65,000 daltons or less.

52. The method of claim 47, wherein the fragment or subfragment has a molecular weight of 55,000 daltons or less.

53. The method of claim 47, wherein the fragment or subfragment has a molecular weight of 50,000 daltons or less.

54. The method of claim 47, wherein said procedure is conducted within 24 hours of the injection of said labeled antibody fragment or subfragment.

55. The method of claim 47, wherein said procedure is a laparoscopic procedure.

56. A method of treatment of lesions, wherein the method comprises:

(a) injecting a patient with composition comprising a divalent single chain antibody fragment or subfragment with a molecular weight of 35,000 Daltons or less, conjugated to an agent capable of being activated to emit Auger electrons or other ionizing radiation, and, optionally, to an agent capable of detection, wherein the antibody conjugate accretes preferentially at the targeted lesion; and

(b) activating said agent capable of being activated, thereby treating said lesions, and, optionally, detecting the optional agent capable of detection.

57. The method of claim 56, wherein the activation and optional detection is during an endoscopic, intravascular, catheter or surgical procedure.

58. The method of claim 56, wherein said procedure is a laparoscopic procedure.

59. The method of claim 56, wherein the activatable agent is a stable element capable of being activated to emit ionizing radiation.

60. The method of claim 56, wherein the activatable agent is a stable element capable of being activated to emit Auger electrons.

61. The method of claim 56, wherein the activatable agent is a halogenated compound.

62. The method of claim 61, wherein the agent is a halogenated pyrimidine.

63. The method of claim 59, wherein the stable element is iodine or indium.

64. The method of claim 56, wherein the activating energy is monochromatic X-rays.

65. The method of claim 64, wherein the monochromatic X-rays emit at an energy of 20-70 keV.

66. The method of claim 65, wherein the monochromatic X-rays emit at an energy of 30-40 keV.

67. The method of claim 56, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation lesion, a clot, hyperplasia and atherosclerotic plaque.

68. The method of claim 56, wherein the fragment or subfragment is monospecific.

69. The method of claim 56, wherein the fragment or subfragment is bispecific.

70. The method of claim 56, wherein the fragment or subfragment has a molecular weight of 65,000 daltons or less.

71. The method of claim 56, wherein the fragment or subfragment has a molecular weight of 55,000 daltons or less.

72. The method of claim 56, wherein the fragment or subfragment has a molecular weight of 50,000 daltons or less.

73. A method of obtaining biopsy samples, wherein the method comprises:

(a) injecting a patient subject to such a procedure parenterally with an effective amount of a labeled antibody fragment or subfragment, which specifically binds an antigen produced by or associated with a lesion;

(b) scanning the accessed interior of the patient at close range with a detection means for detecting the presence of the labeled antibody fragment or subfragment;

(c) locating the sites of accretion of the labeled antibody fragment or subfragment by detecting elevated levels of the labeled antibody fragment or subfragment at such sites with the detection means; and

(d) inserting a biopsy implement into one or more sites of elevated accretion to obtain a biopsy sample, wherein said locating and said biopsy are conducted within 48 hours of the injection.

74. The method of claim 73, wherein the procedure is conducted within 24 hours of the injection.

75. The method of claim 73, wherein the procedure is conducted within 12 hours of the injection.

76. The method of claim 73, wherein the procedure is conducted within 6 hours of the injection.

77. The method of claim 73, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation, a clot, hyperplasia and atherosclerotic plaque.

78. The method of claim 73, wherein the fragment or subfragment is a monoclonal antibody fragment or subfragment.

79. The method of claim 73, wherein the fragment or subfragment is monovalent and selected from the group consisting of an Fv, a single chain antibody, Fab and Fab'.

80. The method of claim 73, wherein the fragment or subfragment is a divalent single chain antibody fragment

or subfragment with a molecular weight of 85,000 daltons or less.

81. The method of claim 73, wherein the fragment or subfragment is bispecific.

82. The method of claim 73, wherein the fragment or subfragment has a molecular weight of 65,000 daltons or less.

83. The method of claim 82, wherein the fragment or subfragment has a molecular weight of 55,000 daltons or less.

84. The method of claim 82, wherein the fragment or subfragment has a molecular weight of 50,000 daltons or less.

85. The method of claim 73, wherein the label for the fragment or subfragment is a radioisotope.

86. The method of claim 85, wherein the radioisotope is selected from the group consisting of technetium-99m, iodine-125, iodine-131, iodine-123, indium-111, and gallium-67.

87. The method of claim 73, wherein the label of said labeled antibody fragment or subfragment is a non-isotopic agent.

88. The method of claim 87, wherein the non-isotopic agent is a photoactive agent.

89. The method of claim 88, wherein the photoactive agent is a fluorescent agent.

90. The method of claim 73, wherein the location of sites of accretion is performed without the use of a clearing agent, contrast agent or subtraction agent.

91. A method of detection of lesions during an endoscopic, laparoscopic, intravascular catheter, or surgical procedure, wherein the method comprises:

(a) injecting a patient who is to undergo such a procedure with a bispecific antibody  $F(ab)$ , or  $F(ab')$ , fragment, wherein the bispecific antibody fragment has a first antibody binding site which specifically binds to an antigen produced or associated with a lesion, and has a second antibody binding site which specifically binds to a hapten, and permitting the antibody fragment to accrete at target sites;

(b) optionally clearing non-targeted antibody fragments using a galactosylated anti-idiotype clearing agent if the bispecific fragment is not largely cleared from circulation within about 24 hours of injection, and injecting a bivalent labeled hapten, which quickly localizes at the target site and clears through the kidneys;

(c) detecting the presence of the hapten by detecting elevated levels of accreted label at the target sites with detection means, within 48 hours of the first injection, and conducting said procedure.

92. The method of claim 91, wherein said antigen produced or associated with a lesion is a tumor- or pathogen-associated antigen.

93. The method of claim 91, further comprising the step of removing lesions at sites of elevated label accretion with a laser or surgically.

94. The method of claim 91, further comprising the step of treating lesions at sites of elevated label accretion with ionizing radiation.

95. The method of claim 91, wherein the procedure is selected from the group consisting of an endoscope, laparoscope, and intravascular catheter procedures, further comprising the step of administering

brachytherapy via the endoscope or catheter to lesions at sites of elevated label accretion.

96. The method of claim 91, wherein the lesion is selected from the group consisting of a cancer, an infectious lesion, an inflammatory lesion, a non-tumorous or noninfectious inflammation lesion, a clot, hyperplasia and atherosclerotic plaque.

97. The method of claim 91, wherein said procedure is a laparoscopic procedure.

98. The method of claim 91, wherein said hapten is labeled with a diagnostic radioisotope, a MRI image enhancing agent or a fluorescent label.